Alabama Medicaid DUR Board Meeting Minutes
July 22, 2009

Members Present: Jimmy Jackson, Clemice Hurst, Kelli Littlejohn, Kevin Royal, Tiffany Minnifield, Christina Faulkner, Bernie Olin, Robert Moon

Members Present via web conferencing: Rhonda Harden, Daniel Mims, Paul Nagrodzki

Members Absent: Denise Thornley-Brown, Paula Thompson, Dan McConaghy, Kevin Green

Kevin Royal, Chairman, called the meeting to order at 1:05pm. Kelli asked members participating via web conferencing to introduce themselves.

Review and Adoption of Minutes of April 22, 2009 meeting: Kevin Royal asked if there were additions, deletions, or changes to the minutes of the April 22, 2009 meeting. Kelli asked that the minutes to the April meeting be corrected to reflect Dan McConaghy's presence. No other changes to the minutes were suggested to the Board. Bernie Olin made a motion to amend the minutes to include Dan McConaghy's name as present. Robert Moon offered a second to the motion. A voice vote in favor of those actions was unanimous.

Christina Faulkner informed the Board that the information requested by Bernie Olin at the last meeting, *Utilization of top 25 drugs by class and claim numbers for the last five years*, will be presented at the next DUR meeting.

Prior Authorization and Overrides Update: Christina Faulkner began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of March, 2009. She reported 8,916 requests and an approval rate of 65.46%. She reported 15,788 electronic requests for the same time frame. From the Prior Authorization and Override Response Time Ratio report for March, 2009, she reported that 70.95% of manual PAs were responded to in less than 2 hours, 90.22% in less than 4 hours and 93.30% in less than 8 hours. Noting the Monthly Manual Prior Authorizations and Overrides report for April, 2009, on page 13, Christina reported 10,273 requests with an approval rate of 66.78% and from page 14, 18,359 electronic requests. From the Response Time Ratio report for April, Christina reported 73.63% of manual PAs responded to in less than 2 hours, 90.78% in less than 4 hours and 94.16% in less than 8 hours.

CMS Annual Report: Christina informed the Board that the Centers for Medicare and Medicaid Services (CMS) DUR Annual Report tracks the Agency's DUR activities and projected cost savings and is required to be submitted to CMS on July 1 of each year by the Agency. Christina reviewed the summary of the report on page 19. The total estimated drug savings for the time period, October 1, 2007 to September 30, 2008, was approximately $140,000. For each $1 spent, the state saved an additional $0.80, or 80%. Due to data issues related to the system changeover to Interchange, only one cycle was run during the fiscal year resulting in a lower than normal cost savings.. For the one cycle, Oct through Dec, 430 letters were sent. Eighty responses were received or approximately 19%. Christina reviewed the Cost Savings table on page 28 and noted a cost savings of 28.36% for single interventions and 44.09% for multiple interventions. An estimated total of 2,404 prescriptions were saved.

Synagis End of Season Report: Christina reviewed the Analysis of Palivizumab Utilization report on page 32. She reported a total number of 9,421 Synagis® claims billed, $15,792,365 reimbursed, and 2050 patients. Christina briefly reviewed the 2008-2009 Synagis® Claims by Month, Top Ten Synagis® PA Denials by Reason and the Top Ten Synagis® Pharmacy Providers. Christina reviewed Synagis® utilization during previous seasons and explained how HID uses this data for trend analysis. Christina then discussed the RSV Data for AL on page 40 and how that relates to the determination of Synagis® season for Medicaid purposes. Kelli Littlejohn informed the Board that the Agency would be presenting a Synagis® web conference on August 14.

Bacterial Conjuntivitis: Christina briefly reviewed bacterial conjunctivitis, its causes and treatments. Christina discussed Alabama utilization data and asked the Board to consider mailing an educational letter to Medicaid providers. Kevin Royal suggested that the Agency consider a recipient newsletter. A discussion followed regarding items of interest that might be included in a newsletter.

RDUR Criteria: Christina presented the set of 45 proposed criteria to the Board for their review. All criteria were approved by written vote of the Board.

Medicaid Update: Tiffany called the board members attention to the PDL and the Alert in their Medicaid packets. She reminded the Board about the upcoming Synagis® web conference August 14 for the upcoming Synagis season. Providers may register by calling the Agency at the number published in the Alert. Tiffany announced that members would be voting for Vice-Chair today. Nominees for Vice-Chair are Denise Thornley-Brown and Kevin Greene. Tiffany instructed members to complete ballots. Kevin Greene was elected as Vice-Chair.

P & T Update: Clemice Hurst began the P & T Update by stating that, in response to the DUR Board's request to ask the P & T Committee to perform a review of Methadone for safety, the issue would be referred to Goold Health for review at the November P & T meeting. Clemice announced that at the last meeting on May 13, Skin and Mucous Membrane Agents were reviewed and Elidel and Protopic were added to the PDL. The next P & T meeting will be held on August 12 in the Board Room and will be conducted via *ilinc* web conferencing feature . The anti-infective agents will be covered and the class will be split between the August 12 meeting and the November 18 meeting. Also on August 12, a new drug review will be presented on Trilipix®. Clemice also stated that in January of 2010 two new classes, PNV and EENT antibacterials, will be added to the PDL.

Next Meeting Date: The next DUR Board meeting will be held on October 28, 2009.

New Business: Kevin Royal, Chairman, asked the Board if there was any new business. There being no new business brought before the Board, Kevin Royal asked for a motion to adjourn. Jimmy Jackson made a motion to adjourn the meeting. The motion was seconded by Bernie Olin. A voice vote to adjourn was unanimous.

Respectfully Submitted,

Christina Faulkner, PharmD

Christina Faulkner, PharmD

ALABAMA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

1. Silodosin / Over-utilization ___✓___ _____ _____

Alert Message: The recommended dose of Rapaflo (silodosin) is 8 mg once daily with a meal.

Conflict Code: ER - Overutilization
Drugs/Disease:

Util A	Util B	Util C (Negating)
Silodosin		Renal Failure (ICD-9s)

Max Dose: 8 mg/day
References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.

2. Silodosin / Over utilization - Renal Impairment ___✓___ _____ _____

Alert Message: The recommended maximum dose of Rapaflo (silodosin) in patients with moderate renal impairment is 4 mg once daily with a meal. Clinical pharmacology studies have shown that plasma concentrations of silodosin are approximately three times higher in patients with moderate renal impairment as compared to subjects with normal renal function. Silodosin use is contraindicated in patients with severe renal impairment. No dosage adjustment is recommended in minor renal impairment.

Conflict Code: ER - Overutilization
Drugs/Disease:

Util A	Util B	Util C (Include)
Silodosin		Severe Renal Impairment (ICD-9s)

Max Dose: 4mg per day
References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.

3. Silodosin / Contraindication ___✓___ _____ _____

Alert Message: Rapaflo (silodosin) is contraindicated in patients with severe renal impairment (CrCl < 30mL/min) and severe hepatic impairment (Child-Pugh score ≥ 10).

Conflict Code: MC - Drug (Actual) Disease Precaution
Drugs/Disease:

Util A	Util B	Util C
Silodosin	Severe Renal Impairment (ICD-9s)	
	Severe Hepatic Impairment (ICD-9s)	
	PhosLo	
	Renagel	
	Zemplar	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

4. Silodosin / Potent CYP3A4 Inhibitors - Contraindication ___✓___ _____ _____

Alert Message: The concurrent use of Rapaflo (silodosin) with potent CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, and ritonavir) is contraindicated. Coadministration of silodosin with these agents may result in significant increases in silodosin plasma concentrations and increase risk of adverse effects due to the inhibition of CYP3A4-mediated metabolism of silodosin.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B		Util C
Silodosin	Ketoconazole	Indinavir	
	Itraconazole	Nefazodone	
	Ritonavir	Nelfinavir	
	Clarithromycin	Saquinavir	
	Atazanavir	Telithromycin	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates.
Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Classification of CYP3A4 Inhibitors. FDA Center for Drug Evaluation and Research. May 1, 2006. Accessed February 02, 2009.
Available at: http://www.fda.gov/cder/drug/drugInteractions/tableSubstrates.htm#PgpTransport

5. Silodosin / Moderate CYP3A4 Inhibitors - Precaution ___✓___ _____ _____

Alert Message: The concurrent use of Rapaflo (silodosin) with moderate CYP3A4 inhibitors (e.g., verapamil, diltiazem and erythromycin) may result in elevated silodosin concentrations due to the inhibition of CYP3A4-mediated silodosin metabolism. Monitor the patient for silodosin adverse effects when co-administering these agents.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B		Util C
Silodosin	Erythromycin	Amprenavir	Aprepitant
	Verapamil	Fluconazole	
	Diltiazem	Fosamprenavir	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates.
Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Classification of CYP3A4 Inhibitors. FDA Center for Drug Evaluation and Research. May 1, 2006. Accessed February 02, 2009.
Available at: http://www.fda.gov/cder/drug/drugInteractions/tableSubstrates.htm#PgpTransport

6. Silodosin / Alpha-Blockers ___✓___ _____ _____

Alert Message: Rapaflo (silodosin), an alpha-1 adrenergic receptor antagonist, should not be used in combination with other alpha-1 blockers. The concurrent use of these agents may have additive effects on blood pressure and increase the risk of adverse effects.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B		Util C
Silodosin	Prazosin	Tamsulosin	
	Terazosin	Alfuzosin	
	Doxazosin		

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

7. Silodosin / Potent P-glycoprotein Inhibitors ___✓___ _____ _____

Alert Message: The concurrent use of Rapaflo (silodosin) with potent P-glycoprotein inhibitors (e.g., ketoconazole, itraconazole, cyclosporine, and quinidine) is not recommended. Silodosin is a P-gp substrate and inhibition of this efflux transporter system may result in significant increases in silodosin exposure.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B		Util C
Silodosin	Ketoconazole	Nelfinavir	
	Itraconazole	Saquinavir	
	Cyclosporine	Verapamil	
	Ritonavir		
	Quinidine		

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates
Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. P-gp Transporters. FDA Center for Drug Evaluation and Research. May 1, 2006. Accessed February 02, 2009.
Available at: http://www.fda.gov/cder/drug/drugInteractions/tableSubstrates.htm#PgpTransport

8. Silodosin / Other Antihypertensive Agents ___✓___ _____ _____

Alert Message: Exercise caution when Rapaflo (silodosin) is used concurrently with antihypertensive agents. The concurrent use of these agents may result in the increased incidence of dizziness and orthostatic hypotension. Monitor patients for adverse effects.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

Util A	Util B	Util C
Silodosin	Beta-Blockers	
	Calcium Channel Blockers	
	Diuretics	
	ACEIs	
	ARBs	
	Antiadrenergic Agents	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, 2009 Gold Standard.

9. Silodosin / PDE-5 Inhibitors ___✓___ _____ _____

Alert Message: Exercise caution when Rapaflo (silodosin) is used concurrently with PDE-5 inhibitors (i.e., sildenafil, tadalafil, and vardenafil). In clinical studies patients receiving silodosin and a PDE-5 inhibitor had a higher total number of positive orthostatic test results compared to patients on silodosin alone.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

Util A	Util B	Util C
Silodosin	Sildenafil	
	Tadalafil	
	Vardenafil	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, 2009 Gold Standard.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

10. Milnacipran / Over-utilization ___✓___ _____ _____

Alert Message: The recommended dose of Savella (milnacipran) is 100 mg per day given in two divided doses. Milnacipran therapy should always begin with dosing at 12.5 mg and increase to 100 mg per day over a 1-week period. The daily dose may be increased to 200 mg per day based on individual response.

Conflict Code: ER - Overutilization

Drugs/Diseases		
Util A	Util B	Util C
Milnacipran		

Max Dose: 200 mg per day

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

11. Milnacipran / Nonadherence ___✓___ _____ _____

Alert Message: Non-adherence to the prescribed dosing regimen for Savella (milnacipran) may result in loss of therapeutic effect.

Conflict Code: LR – Non-adherence

Drugs/Diseases		
Util A	Util B	Util C
Milnacipran		

Less than 75 days in 90 day review.

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

12. Milnacipran / Monoamine Oxidase Inhibitors ___✓___ _____ _____

Alert Message: The concurrent use of Savella (milnacipran) and a monoamine oxidase inhibitor (MAOI) is contraindicated. Milnacipran has serotonin reuptake inhibitor activity and the use of this agent with a MAOI may cause a rapid, excessive accumulation of serotonin resulting in serious, sometimes fatal, reactions. Milnacipran should not be used within 14 days of discontinuing an MAOI and at least 5 days should elapse after stopping milnacipran before starting an MAOI.

Conflict Code: DD- Drug/Drug Interaction

Drugs/Diseases		
Util A	Util B	Util C
Milnacipran	Isocarboxazid Tranylcypromine Phenelzine	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

13. Milnacipran / Risk of Suicide (Black Box Warning) ___✓___ _____ _____

Alert Message: Savella (milnacipran) is a selective serotonin and norepinephrine reuptake inhibitor (SNRI), similar to some drugs used for the treatment of depression and other psychiatric disorders. SNRIs may increase the risk compared to placebo of suicidal thinking and behavior in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders. Monitor patients closely for unusual changes in behavior.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Milnacipran		

References:
Savella Prescribing Information, Jan 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

14. Milnacipran / Uncontrolled Narrow Angle Glaucoma ___✓___ _____ _____

Alert Message: The use of Savella (milnacipran) is contraindicated in patients with uncontrolled narrow angle glaucoma. In clinical trials, milnacipran was associated with an increased risk of mydriasis. Milnacipran is a selective serotonin/norepinephrine reuptake inhibitor and mydriasis has been reported with other dual reuptake inhibitors agents.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Narrow Angle Glaucoma	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

15. Milnacipran / Serotonergic Drugs ___✓___ _____ _____

Alert Message: The concurrent use of Savella (milnacipran) and a serotonergic drug is not recommended. Milnacipran is a selective serotonin/norepinephrine reuptake inhibitor and concomitant therapy with other serotonergic drugs may cause accumulation of serotonin and increase the risk of serotonin syndrome (e.g., mental status changes, hypertension, vasoconstriction, and neuronal aberrations).

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Milnacipran	Triptans	TCAs	
	Tramadol	Mirtazapine	
	SSRIs	Bupropion	
	SNRIs	Trazodone	
	Nefazodone	Codeine	
	Fentanyl	Zyvox	
	Lithium		

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

16. Milnacipran / Clonidine ___✓___ _____ _____

Alert Message: Concurrent use of Savella (milnacipran) and clonidine may result in the loss of blood pressure control. Clonidine acts to decrease norepinephrine (NE) release in the brain which leads to a reduction in arterial blood pressure. Milnacipran inhibits NE reuptake, thereby increasing NE levels and inhibiting the effects of clonidine.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Clonidine	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

17. Milnacipran / Seizures ___✓___ _____ _____

Alert Message: Savella (Milnacipran) should be used with caution in patients with a history of seizure disorders. Seizures have been reported, infrequently, in patients treated with milnacipran for disorders other than fibromyalgia.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Seizures	
	Epilepsy	
	Convulsions	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

18. Milnacipran / Hypertension ___✓___ _____ _____

Alert Message: Savella (milnacipran) may cause elevated blood pressure and heart rate. Monitor blood pressure and heart rate prior to initiating milnacipran therapy and periodically throughout treatment.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Hypertension ICD-9	
	Beta Blockers	
	ACE Inhibitors	
	ARBs	
	Diuretics	
	Calcium Channel Blockers	
	Antiadrenergic Agents - Centrally Acting & Peripherally	
	Peripheral Vasodilators	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

19. Febuxostat / Over utilization ___✓___ _____ _____

Alert Message: The recommended starting dose of Uloric (febuxostat) is 40 mg once daily and may be increased to 80 mg once daily in patients who do not achieve a serum uric acid (sUA) less than 6 mg per dL after 2 weeks with the 40 mg. Exceeding the recommended daily dose may increase the risk of adverse effects (e.g., rash, arthralgia, nausea, and liver function abnormalities).

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

Max Dose: 80 mg per day

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

20. Febuxostat / Nonadherence ___✓___ _____ _____

Alert Message: Non-adherence to the prescribed dosing regimen for Uloric (febuxostat) may result in loss of therapeutic effect.

Conflict Code: LR – Underutilization
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

Less than a 75 day supply in 90 days

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

21. Febuxostat / Azathioprine, Mercaptopurine & Theophylline ___✓___ _____ _____

Alert Message: Uloric (febuxostat) is contraindicated in patients being treated with drugs metabolized by xanthine oxidase (i.e., azathioprine, mercaptopurine, and theophylline). Febuxostat is a xanthine oxidase (XO) inhibitor and concurrent use of febuxostat with drugs metabolized by XO may cause substantially increased plasma concentrations of the XO metabolized drug leading to severe toxicity.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Febuxostat	Azathioprine Mercaptopurine Theophylline	

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

22. Febuxostat / Cardiovascular Events (Warning) ___✓___ _____ _____

Alert Message: In clinical trials, patients treated with Uloric (febuxostat) had a higher rate of cardiovascular thromboembolic events than allopurinol-treated patients. Monitor patients for signs and symptoms of MI or stroke.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

23. Febuxostat / Liver Enzyme Elevation (Warning) ___✓___ _____ _____

Alert Message: It is recommended that patients receiving Uloric (febuxostat) receive laboratory assessment of liver function at 2 and 4 months following initiation of febuxostat and periodically thereafter. In controlled studies, elevated transaminase elevations were observed and were the most common adverse event that led to discontinuation of the drug.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

24. Metoclopramide / Black Box Warning ___✓___ _____ _____

Alert Message: Chronic and high-dose use of metoclopramide has been linked to tardive dyskinesia even after the drug is discontinued. These adverse effects are rarely reversible and have no known treatment. The patients at greatest risk are the elderly, especially older women, patients who have been on the drug for a long time and patients taking higher doses. The chronic use of metoclopramide should be avoided in all but rare cases where the benefit outweighs the risk and patients should be informed of the risk.

Conflict Code: TA - Therapeutic Appropriateness **(Black Box Warning)**
Drugs/Diseases

Util A	Util B	Util C
Metoclopramide		

References:
MedWatch: FDA Safety Information and Adverse Event Reporting Program, 2009.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

25. Zonisamide / Therapeutic Appropriateness ___✓___ _____ _____

Alert Message: Treatment with zonisamide can cause metabolic acidosis. Patients at greater risk for developing metabolic acidosis are those with predisposing conditions or therapies (e.g. renal disease, severe respiratory disease, diarrhea, ketogenic diet or certain drugs). The risk appears to be more frequent and severe in younger patients. Measure serum bicarbonate before starting zonisamide treatment and periodically during treatment with zonisamide, even in the absence of symptoms.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Zonisamide		

References:
MedWatch: FDA Safety Information and Adverse Event Reporting Program, 2009.

26. Metoclopramide /Therapeutic Appropriateness ___✓___ _____ _____

Alert Message: The safety and effectiveness of metoclopramide in pediatric patients has not been established. Dystonias and other extrapyramidal reactions associated with metoclopramide are more common in the pediatric population than in adults. Both the risk of developing metoclopramide-induced tardive dyskinesia and the likelihood it will become irreversible are believed to increase with the duration of treatment and the total cumulative dose.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Metoclopramide		

Age Range: 0 – 17 years of age

References:
Clinical Pharmacology, Gold Standard Media 2009.
Facts & Comparisons, 2009 Updates.
Reglan Prescribing Information, Feb. 2004, Schwarz Pharma.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

27. Metoclopramide / Meds Causing Extrapyramidal Symptoms ____✓____ _____ _____

Alert Message: Metoclopramide is contraindicated in patients receiving other drugs that are likely to cause extrapyramidal reactions. The concurrent use of these agents may increase the frequency or severity of these reactions.

Conflict Code: DD – Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Metoclopramide	Antidepressants	Phenytoin	
	Antipsychotics	Reserpine	
	Valproic Acid	Amiodarone	
	Promethazine		
	Methylphenidate		
	Amphetamines		
	Methamphetamine		
	Prochlorperazine		

References:
Clinical Pharmacology, Gold Standard Media 2009.
Facts & Comparisons, 2009 Updates.
Reglan Prescribing Information, Feb. 2004, Schwarz Pharma.
Moses S. Drug-Induced Movement Disorders. April 2008. Family Practice Notebook.
Available at: http://www.fpnotebook.com/Neuro/Pharm/DrgIndcdMvmntDsrdrs.htm
Factor SA, Leffler JB, Murray CF, Drug-induced Movement Disorders: A Clinical Review CME.
Medscape CME. 2009. Available at: http://www.medscape.com/viewprogram/18880_pnt

28. Clopidogrel / Proton Pump Inhibitors _____✓____ _____ _____

Alert Message: Some recent studies suggest a possible interaction if clopidogrel (Plavix) is given concurrently with a proton pump inhibitor (PPI). Coadministration of these agents may cause decreased clopidogrel anti-platelet efficacy which may lead to an increased incidence of adverse cardiovascular events. Monitor these patients closely for loss of clopidogrel efficacy. Current ACC/ACF/AHA guidelines have not changed and a PPI is still recommended for gastroprotection in patients receiving clopidogrel and NSAIDS who are at high risk for GI bleeds.

Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Clopidogrel	Omeprazole	
	Esomeprazole	
	Lansoprazole	
	Pantoprazole	
	Rabeprazole	
	Dexlansoprazole	

References:
Aubert RE et al. Proton pump inhibitors effect on clopidogrel effectiveness: the clopidogrel Medco outcomes study (abstract 3998). Circulation. 2008;118:S815.
Dunn SP et al. Baseline proton pump inhibitor use is associated with increased cardiovascular events with and without use of clopidogrel in the CREDO trial (abstract 3999). Circulation. 2008;118:S815.
American Heart Association. American College of Cardiology (ACC)/American College of Gastroenterology (ACG)/American Heart Association (AHA) Joint Committee on Studies Regarding Possible Interaction of Clopidogrel and Proton Pump Inhibitors. Available at: http://americanheart.mediaroom.com/index.php?s=43&item=611&printable Accessed January 1, 2009.
Do proton pump inhibitors decrease clopidogrel activity? Pharmacist Letter/Prescriber's Letter 2008;24(11):241114.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

29. Orlistat / Levothyroxine ____✓____ _____ _____

Alert Message: Hypothyroidism has been reported in patients treated concomitantly with Xenical (orlistat) and levothyroxine. Orlistat may decrease the absorption of levothyroxine resulting in subtherapeutic levels. Patients treated concurrently with these agents should be monitored for changes in thyroid function and advised to take levothyroxine and orlistat at least 4 hours apart.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Orlistat	Levothyroxine	

References:
Xenical Prescribing Information, Jan. 2009, Roche Laboratories Inc.
Synthroid Prescribing Information, July 2008, Abbott Laboratories.

30. Orlistat / Cyclosporine ____✓____ _____ _____

Alert Message: The use of (Xenical) orlistat should be avoided in patients receiving cyclosporine therapy. Orlistat may decrease the absorption of cyclosporine resulting in decreased cyclosporine blood levels and subtherapeutic effects. If concurrent use of these agents is warranted advise the patient to take cyclosporine at least 2 hours before or after orlistat.

Conflict Code: DD – Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Orlistat	Cyclosporine	

References:
Xenical Prescribing Information, Jan. 2009, Roche Laboratories Inc.
Facts & Comparisons, 2009 Updates.

31. Orlistat / Warfarin ____✓____ _____ _____

Alert Message: Patients on chronic stable doses of warfarin who are prescribed Xenical (orlistat) should be monitored closely for changes in coagulation parameters. Orlistat therapy tends to cause a decrease in vitamin K absorption thereby increasing the anticoagulant effect of warfarin.

Conflict Code: DD – Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Orlistat	Warfarin	

References:
Xenical Prescribing Information, Jan. 2009, Roche Laboratories Inc.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

32. Clarithromycin & Azithromycin / Myasthenia Gravis ___✓___ _____ _____

Alert Message: Exacerbations of symptoms of myasthenia gravis and new onset of myasthenia syndrome have been reported in patients receiving clarithromycin or azithromycin therapy.

Conflict Code: DD – Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Clarithromycin	Myasthenia Gravis	
Azithromycin		

References:
Biaxin Prescribing Information, Oct. 2008 Abbott Laboratories.
Zithromax Prescribing Information, Jan. 2009, Pfizer Labs.

33. Erythromycin / Myasthenia Gravis ___✓___ _____ _____

Alert Message: Erythromycin may aggravate the muscle weakness in patients with myasthenia gravis.

Conflict Code: MC – Drug/Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Erythromycin	Myasthenia Gravis	

References:
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, Gold Standard 2009.

34. Itraconazole / Heart Failure ___✓___ _____ _____

Alert Message: Do not administer itraconazole for the treatment of onychomycosis in patients with evidence of ventricular dysfunction such as CHF or a history of CHF. If signs or symptoms of CHF occur during administration of itraconazole discontinue administration.

Conflict Code: MC – Drug/Disease Precaution **(Black Box Warning)**
Drugs/Diseases

Util A	Util B	Util C
Itraconazole	Heart Failure	Onychomycosis

References:
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, Gold Standard 2009.
Sporanox Prescribing Information, April 2008, Janssen/Ortho-McNeil Pharmaceuticals, Inc.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

35. Fesoterodine / High Dose ___✓___ _____ _____

Alert Message: The recommended starting dose of Toviaz (fesoterodine) is 4 mg once daily. Based upon individual response and tolerability, the dose may be increased to 8 mg once daily. Exceeding the recommended dose may increase the risk of adverse anticholinergic effects (e.g. constipation, dry mouth, dry eyes, and urinary retention).

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C (Negating)	
Fesoterodine		Severe Renal Impairment	Telithromycin
		Ketoconazole	Saquinavir
		Itraconazole	Ritonavir
		Clarithromycin	Nelfinavir
		Nefazodone	Atazanavir

Max Dose: 8 mg per day

References:
Toviaz Prescribing Information, April 2008, Pfizer Labs.
Facts & Comparisons, 2009 Updates.

36. Fesoterodine / High Dose ___✓___ _____ _____

Alert Message: The daily dose of Toviaz (fesoterodine) should not exceed 4 mg once daily in patients with severe renal insufficiency (CrCL < 30mL/min) and patients on potent CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, and clarithromycin).

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C (Inclusive)
Fesoterodine		Sever Renal Impairment
		Ketoconazole
		Itraconazole
		Clarithromycin

Max Dose: 4 mg per day

References:
Toviaz Prescribing Information, April 2008, Pfizer Labs.
Facts & Comparisons, 2009 Updates.

37. Fesoterodine / Therapeutic Appropriateness ___✓___ _____ _____

Alert Message: Toviaz (fesoterodine) has not been studied in patients with severe hepatic impairment and its use is not recommended in this patient population.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Fesoterodine	Hepatic Coma	
	Cirrhosis	
	Chronic Hepatitis	
	Porphyria	

References:
Toviaz Prescribing Information, April 2008, Pfizer Labs.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

38. Fesoterodine / Contraindications ____✓____ _____ _____

Alert Message: Toviaz (fesoterodine) is contraindicated in patients who have urinary retention, gastric retention, and uncontrolled narrow-angle glaucoma. Fesoterodine is a muscarinic receptor antagonist and use of this agent would exacerbate the above conditions.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Fesoterodine	Urinary Retention	
	Gastric Retention	
	Uncontrolled Narrow-Angle Glaucoma	

References:
Toviaz Prescribing Information, April 2008, Pfizer Labs.
Facts & Comparisons, 2009 Updates.

39. Fesoterodine / Precautions ____✓____ _____ _____

Alert Message: Caution should be exercised if Toviaz (fesoterodine) is prescribed in patients who have bladder outlet obstruction, decreased gastric motility, controlled narrow-angle glaucoma, and myasthenia gravis. Fesoterodine is a muscarinic receptor antagonist and use of this agent may exacerbate these conditions.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Fesoterodine	Bladder Outlet Obstruction	
	Decreased Gastric Motility	
	Controlled Narrow-Angle Glaucoma	
	Myasthenia Gravis	

References:
Toviaz Prescribing Information, April 2008, Pfizer Labs.
Facts & Comparisons, 2009 Updates.

40. Fesoterodine / Anticholinergic Agents ____✓____ _____ _____

Alert Message: Concomitant use of Toviaz (fesoterodine) and an anticholinergic drug may increase the frequency and/or severity of anticholinergic-like effects (e.g. constipation, dry mouth, urinary retention). Anticholinergic agents may potentially alter the absorption of some coadministered drugs because of anticholinergic effects on GI motility.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B				Util C
Fesoterodine	Hyoscyamine	Propantheline	Scopolamine	Milnacipran	
	Biperiden	Glycopyrrolate	Antihistamines	Antipsychotics	
	Trihexyphenidyl	Atropine	TCAs	Meclizine	
	Ipratropium	Belladonna	Mirtazapine	Cyclizine	
	Benztropine	Mepenzolate	Venlafaxine		
	Dicyclomine	Methscopolamine	Desvenlafaxine		

References:
MacDiarmid SA. Concomitant Medications and Possible Side Effects of Antimuscarinic Agents. Rev Urol 2008 Spring, 10(2): 92-98.
Toviaz Prescribing Information, April 2008, Pfizer Labs.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

41. Fesoterodine / Weak & Moderate CYP3A4 Inhibitors ___✓___ _____ _____

Alert Message: In patients taking weak or moderate CYP3A4 inhibitors (e.g. erythromycin, diltiazem, and cimetidine) with Toviaz (fesoterodine) careful assessment of tolerability at the 4 mg daily dose is advised prior to increasing the daily dose to 8 mg. While this specific interaction potential was not examined by clinical study, some pharmacokinetic interaction is expected, albeit less then that observed with potent CYP3A4 inhibitors.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A	Util B	Util C
Fesoterodine	Erythromycin	
	Aprepitant	
	Diltiazem	
	Fluconazole	
	Fosamprenavir	
	Verapamil	

References:

Toviaz Prescribing Information, April 2008, Pfizer Labs.
Facts & Comparisons, 2009 Updates.

Note: Toviaz is included in the existing Therapeutic Duplication criteria for the Overactive Bladder Medications.

42. NSAIDS / Diabetes ___✓___ _____ _____

Alert Message: NSAIDS should be used with caution in diabetic patients due to the increased risk of renal toxicity. Diabetes is a risk factor for renal insufficiency and the use of NSAIDs can cause a dose-dependent reduction in prostaglandin formation by the kidneys resulting in decreased renal perfusion and ischemic injury.

Conflict Code: DB – Drug Disease Precaution

Drugs/Diseases

Util A	Util B	Util C
NSAIDS	Diabetes ICD-9s	Rosiglitazone
Celebrex	Insulins	Pioglitazone
	Chlorpropamide	Repaglinide
	Tolazamide	Nateglinide
	Tolbutamide	Pramlintide
	Glipizide	Exenatide
	Glimepiride	Sitagliptin
	Glyburide	Acarbose
	Miglitol	

References:

Rifkin BD, Perazella MA. Analgesic Therapy in Patients with Chronic Kidney Disease: A Case-Based Approach. Hospital Physician May 2005: 43;13-22.
Facts & Comparisons, 2009 Updates.
FDA CDER Alert: Acetaminophen Hepatotoxicity and Nonsteroidal Anti-Inflammatory Drugs (NSAID)-related Gastrointestinal and Renal Toxicity; Letter to State Boards of Pharmacy. Jan. 2004.
Available at: http://www.fda.gov/cder/drug/analgesics/letter.htm

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*

43. NSAIDS / Pain in Older Patients ___✓___ _____ _____

Alert Message: In older patients acetaminophen should be considered as initial and ongoing pharmacotherapy in the treatment of persistent pain, particularly musculoskeletal pain, owing to its demonstrated effectiveness and good safety profile. Nonselective NSAIDS and COX-2 inhibitors may be considered rarely, and with extreme caution, in highly selected individuals. All patients with moderate to severe pain, pain-related functional impairment or diminished quality of life due to pain should be considered for opioid therapy, which may be safer than long-term use of NSAIDS.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C (Negating)
NSAIDS		Acetaminophen
Celebrex		Liver Failure/Hepatic Insufficiency
		Alcohol Abuse/Dependence

Age Range: 55 and older

References:
American Geriatric Society (AGS) Clinical Practice Guideline: Pharmacological Management of Persistent Pain in Older Persons. American Geriatrics Society.
Available online: http://www.americangeriatrics.org/education/final_recommendations.pdf

44. Pimozide / Citalopram & Escitalopram ___✓___ _____ _____

Alert Message: The concurrent use of pimozide with citalopram or escitalopram is contraindicated. Concomitant use of these agents may result in QT prolongation and life-threatening cardiac arrhythmias.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Pimozide	Citalopram	
	Escitalopram	

References:
Orap Prescribing Information, Jan. 2009, Gate Pharmaceuticals.
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, 2009 Gold Standard.

Criteria Recommendations	*Approved*	*Approved As Amended*	*Rejected*
45. Oral Antihyperglycemics / Insulin Negating	✓		

Alert Message: The patient is receiving multiple oral antihyperglycemic medications with no evidence of insulin therapy. The ADA/EASD Consensus Statement on Medical Management of Hyperglycemia recommends the early addition (Tier 1-Step 2) of insulin therapy in patients who do not achieve and/or sustain target goals. If appropriate for this patient consider modifying the patient's regimen to include insulin.

Conflict Code: TD – Therapeutic Duplication (3 or more OAD)
Drugs/Disease

Util A	Util B	Util C (Negating)
Rosiglitazone		Insulins
Pioglitazone		
Chlorpropamide		
Repaglinide		
Nateglinide		
Tolazamide		
Tolbutamide		
Pramlintide		
Glipizide		
Glimepiride		
Glyburide		
Acarbose		
Miglitol		
Sitagliptin		
Exenatide		

References:
Nathan DM, Buse JB, Davidson, MT et al. Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy – A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. Jan. 2009; 32(1):193-203.
The Case for Early Insulin Use in Type 2 Diabetics.

The minutes of the July 22, 2009 DUR Board Meeting have been reviewed and approved as submitted.

Carol H. Steckel, Commissioner — (✓) Approve ( ) Deny — 9/11/09 Date

Kathy Hall, Deputy Commissioner — (✓) Approve ( ) Deny — 9/9/09 Date

Robert Moon, M.D., Medical Director — (✓) Approve ( ) Deny — 9-16-09 Date